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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/904,786      | 07/12/2001  | Avi Ashkenazi        | 10466/84            | 3015             |

35489 7590 08/11/2005

HELLER EHRMAN LLP  
275 MIDDLEFIELD ROAD  
MENLO PARK, CA 94025-3506

EXAMINER

BASI, NIRMAL SINGH

|          |              |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1646

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/904,786

Applicant(s)

ASHKENAZI ET AL.

Examiner

Nirmal S. Basi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 17 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 39-43 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 39-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. Amendment filed 5/17/05 has been entered. Claims 39-43 are pending and under examination in this office action. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

#### *Claim Rejections Maintained*

2. The rejection of claims 39-43 under 35 U.S.C. 112, first paragraph, as lacking enablement is maintained for reasons of record in the office actions of 11/17/04, 4/28/04 and 12/19/03.

Applicants argue that the MLR assay is a well accepted and useful assay for identifying immunostimulants and is a widely used proliferative assay of T-cell function and can identify agents that can boost the immune system. Dr. Fong points to IL-12 as such a stimulant and states that a PRO polypeptide that stimulates T-cell proliferation with an activity "at least 180% of control" would find practical utility as an immune stimulant. Applicants submit that PRO335, contributes to stimulating the cellular responses (cellular immunity) rather than the humoral responses, of the immune system and therefore, is not directed to any "particular antigen". Applicant further argues the MLR assay is useful for detecting immunostimulatory activities of molecules like PRO335.

Applicants' arguments have been fully considered but have not been found to be persuasive. No "particular antigen" is identified in the specification; there is no guidance

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as to how PRO335 could be used to boost the response to any antigen. Current Protocols in Immunology states on p. 3.12.11 that the MLR “only detects dividing cells instead of measuring true effector T-cell function” and that it is “not clear which T cell function is measured in proliferative assays”, and further that “the proliferative response should be used solely as a general indicators of T cell reactivity”. Data obtained might variously reflect proliferation of CTL, lymphokine producing T cells, or non-activated bystander cells and will be severely affected by the function of non-T cells. Differences in responsiveness in a proliferative assay in part reflect differences in IL-2 production, according to Current Protocols in Immunology. As has been stated previously, the MLR measures the reactivity of one individual to another and is, as Current Protocols in Immunology states, highly variable. Current Protocols in Immunology in fact describes many variables that must be controlled for. In the instant application, no such controls, such as for maximum response or for the inherent variability of individual responses, are provided. There is no indication of the statistical significance of the results. There are no autologous controls. No correlation is provided to any particular *in vivo* function; there is no guidance to indicate that PRO335 could be used to any therapeutic effect for the treatment of diseases such as cancer or HIV. The references cited by Applicant fail to provide compensatory guidance. Steinman and Thurner et al. (see previous office action) address the utility of dendritic cells but not of a stimulatory MLR. Gubler (see previous office action) describes the identification of the molecule IL-12 but uses the MLR merely to compare activities, not as the basis for describing a molecule as a therapeutically useful immunostimulant. The subsequent research of Peterson et al.

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(see previous office action) was clearly required to suggest that the molecule could be used in this fashion. Thus, without further guidance correlating the observed stimulatory activity to a particular, useful property, it would require undue experimentation to use PRO335.

NO CLAIM IS ALLOWED.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on 571-272-0829. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nirmal S. Basi  
ART Unit 1646  
8/8/05

*ns*

*Joseph T. R.*  
**JOSEPH MURPHY**  
**PATENT EXAMINER**